

# USER'S GUIDE

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The Cancer Drug Manual provides concise, evaluative drug information on drugs used in an oncology setting. The first edition of the Cancer Drug Manual was published by BCCA in 1990, followed by a complete revision in 1994. Since 2001, the Cancer Drug Manual has become a continuously updated BCCA website resource. Documents prepared after 1994 follow a different template format in order to incorporate a number of new features, including fully referenced citations in lieu of a bibliography. All monographs will eventually be updated using this new format.

Drug monographs and patient handouts are arranged alphabetically by generic name and indexed separately. Basic information for the preparation and stability of parenteral benefit drugs and drugs approved for use at the BCCA is found in the Chemotherapy Preparation and Stability Chart, created in 2006. The Hazardous Drug List, created in 2010, identifies those drugs which will be handled as hazardous at the BCCA.

## **CANCER DRUG MANUAL DRUG MONOGRAPH:**

Each drug monograph contains the following sections:

### **DRUG NAME:**

- Generic name as listed in the Compendium of Pharmaceutical Specialties.

### **SYNONYM(S):**

- Includes alternate generic names used in Canada and the US as well as abbreviations; use of synonyms is discouraged for writing prescriptions in favour of the full generic name of the drug.

### **COMMON TRADE NAMES:**

- Trade names used in Canada and the US.

### **CLASSIFICATION:**

- General pharmacologic classification.

### **MECHANISM OF ACTION:**

- Brief description of the mechanism of action to provide the rationale for drug choice and to help predict the effect and toxicity of a drug.

### **PHARMACOKINETICS:**

- Brief description of pharmacokinetic data to help predict the effect and toxicity of a drug, including any known variability affected by patient factors (e.g., gender, age, ethnicity). Numeric data are presented as mean  $\pm$  standard deviation unless otherwise specified.

### **USES:**

- Includes only malignant conditions that may be treated with this drug.
- Health Canada approved indications and common unlabelled indications may be included.  
NOTE: Inclusion of an indication in this section does not imply that it is a BCCA approved indication.

## SPECIAL PRECAUTIONS:

- Includes special considerations for identifying patients who should NOT receive a drug, or should receive it with cautions or dose adjustment. NOTE: these are *special* considerations; we have not stated the obvious. For example, none of these drugs should be used in patients known to be hypersensitive to them. Similarly, patients being treated with immunosuppressive agents should not receive live virus vaccinations. Immunosuppressive agents should probably not be administered during active viral infection (e.g., chicken pox, herpes zoster) because of the risk of developing more severe disease.
- Readers are also alerted to the risks of chemotherapy on carcinogenicity, mutagenicity, fertility, pregnancy and breastfeeding.

## SIDE EFFECTS:

- Includes adverse events that may present during drug treatment but do not necessarily have a causal relationship with the drug, and adverse reactions that may be suspected to be related to the drug.<sup>1,2</sup>
- Side effects are presented in table format; selected side effects may be described in greater details in paragraphs after the table.
- Side effects are categorised according to the US National Cancer Institute *Common Terminology Criteria for Adverse Events (CTCAE)* and *Common Toxicity Criteria (CTC)*,<sup>1</sup> with the exception of febrile neutropenia which is included in the *blood/bone marrow* category for ease of cross-reference between course of neutropenia and infection.
- Inclusion of side effects is based on the following:
  - unintended effects related to the pharmacology (side effects) or noxious and unintended responses to the drug (adverse drug reactions).<sup>2</sup>
  - case reports showing at least possible causal association<sup>2</sup> and collaborated with other investigations (e.g., pharmacokinetic evidence).<sup>3</sup>
  - reported frequency of > 1% in the product monograph or pivotal trials.<sup>3</sup> For data arising from placebo-controlled trials, side effects are generally included if the reported frequency was > 5% higher than the placebo group.
  - rare side effects that are potentially life-threatening, more commonly reported in related drugs, or of special interest to cancer patients (e.g., alopecia).
- Other features of the table include:
  - *Extravasation hazard* is classified as vesicant, irritant, or none. See Extravasation Policy in the Appendix for definitions.
  - *Emetogenic potential* is classified according to the percentage of patients who will vomit without antiemetics: high (> 90%); high moderate (60-90%); low moderate (10-60%); non-emetogenic (< 10%). See BCCA Protocol SCNausea: Guidelines for Prevention and Treatment of Chemotherapy-induced Nausea and Vomiting in Adults.
  - Frequency for overall (all grades) and severe (grade 3 or 4) side effects are reported when known.
  - Onset of side effects: assignment of onset has been discontinued in monographs developed or revised after July 2006. Onset of side effects was coded as immediate (hours to 7 days); early (1 to 4 weeks); delayed (1 to 3 months); or late (more than 3 months) in some older monographs. NOTE: where included, onset is usually an estimate by the Cancer Drug Manual writer as onset is rarely fully described in the literature.
  - Clinically significant or dose limiting side effects (previously *underlined*) are in ***bold and italics*** in monographs prepared after 1994.

## INTERACTIONS:

- Evidence-based drug-drug, drug-herb, drug-food, and drug-lab interactions are listed in the interaction table, including details regarding the outcome of the interaction, mechanism, and management strategy.
- Interactions due to obvious, simple additive or antagonistic effects based on known pharmacologic activity of the interacting agents are NOT usually included.<sup>4</sup>
- Theoretical interactions are included below the interaction table.
- Data from *in vitro* studies of cytochrome P-450 enzymes are included as their clinical utility is increasingly recognised by regulatory authorities.<sup>5,6</sup>
- Grapefruit interactions are included; however, interactions with other foods susceptible to interaction (i.e., pomelo, lime, bitter orange, etc.) are not routinely included as this information is not readily available in standard references and the clinical significance is unknown.
- Readers are encouraged to speculate about potential interactions, especially for new agents. Extreme caution and vigilance should prevail if drugs used in combination share a metabolic pathway with the cytotoxic drug in question or where one is highly plasma protein bound and has a narrow therapeutic range.

## SUPPLY AND STORAGE:

- Identifies available pharmaceutical products and proper storage; includes inactive ingredients of potential clinical significance.<sup>7-9</sup>
- For basic information on the current brand used at the BC Cancer Agency, refer to Chemotherapy Preparation and Stability Chart for details.

## SOLUTION PREPARATION AND COMPATIBILITY:

- Identifies information pertinent to the safe preparation of the drug.
- For basic information on preparation and administration of the current brand used at the BCCA, refer to Chemotherapy Preparation and Stability Chart for details.
- For details relating to physicochemical compatibility details, readers should consult current specialty references dealing specifically with injectable drugs.

## PARENTERAL ADMINISTRATION:

- Includes commonly used routes and rates of administration, as well as routes that are relatively or absolutely contraindicated.
- BCCA recommended routes and rates of administration are in ***bold and italics***.
- Routes not in common use are preceded with the term "investigational".

## DOSAGE GUIDELINES:

- Includes the most common average dosage range and routes of administration; usual dosing regimens used at BCCA are in ***bold and italics***.
- Provides the common dosing regimens used without support by colony stimulating factors and other cytokines.
- Inclusion of a dosing regimen in this section does not imply efficacy or safety for a particular indication. Readers should always refer to the protocol by which a patient is being treated.
- Dosing regimens information is generally based on the recommendations of the US National Institutes of Health and National Cancer Institute<sup>10</sup>:
  - cycle length (except chronic daily dosing, e.g., tamoxifen),
  - dosage (usually expressed per body surface area or weight),
  - amount of drug per dose and range,
  - frequency of administration and/or days on which the drug is given,
  - total dose per cycle and range, and
  - any other information pertinent to the safe administration of the drug.

- additional information such as maximum lifetime dose, dose modifications for toxicity or disease states (e.g., renal failure, hepatic failure), and children's doses.

#### **REFERENCES:**

- Identifies cited references used in the writing of the monograph.
- Replaces the Bibliography in previous editions of the Cancer Drug Manual.

#### **CANCER DRUG MANUAL PATIENT HANDOUT: FOR THE PATIENT**

- Briefly describes how a drug works, how it is administered, and identifies information that a patient needs to know to identify, predict, prevent or manage side effects.
- Includes a side effect table for side effects having a reported incidence of 10% or more. A brief description of clinical manifestations and suggested management strategy is included. Rare, but serious side effects are included after the side effect table.
- Information provided after the side effect table is intended to help the patient identify symptoms which are considered medical emergencies and those which should be reported to the doctor in a timely manner.
- Long-term effects, such as risk of secondary cancers, are not generally included.

#### **CANCER DRUG MANUAL "INTERIM" DRUG MONOGRAPH:**

Interim monographs are provided for parenteral non-benefit antineoplastic drugs which are made available at BCCA through the BCCA Compassionate Access Program, including drugs which are not yet marketed in Canada and are accessible through the Health Canada Special Access Program. Drug information is necessary to ensure the safe preparation and administration of the drug at BCCA. Due to the nature of CAP requests, this information is developed in an expedited fashion and is expected to be utilized only for a small population of patients. Therefore, unlike the full CDM drug monograph, interim monographs are limited in scope and only provide information related to dosing, preparation, administration, and toxicity. See BCCA Policy III-90: Parenteral Drug Therapy Policy.

Each interim drug monograph contains the following sections:

##### **DRUG NAME:**

- Depending on the country of origin, generic name as listed in the Compendium of Pharmaceutical Specialties, US Food and Drug Administration, or European Medicines Agency.

##### **SYNONYM(S):**

- Includes alternate generic names used in Canada and the US as well as abbreviations; use of synonyms is discouraged for writing prescriptions in favour of the full generic name of the drug.

##### **COMMON TRADE NAME(S):**

- Trade names used in Canada and the US (if available).

##### **CLASSIFICATION:**

- General pharmacologic classification.

### MECHANISM OF ACTION:

- Brief description of the mechanism of action to provide the rationale for drug choice and to help predict the effect and toxicity of a drug.

### USES:

- Includes only malignant conditions that may be treated with this drug.
- Health Canada approved indications and common unlabelled indications are included if applicable; however monographs may also be created for drugs which are not marketed in Canada. Note: drugs available through the Health Canada Special Access Program (and approved at BCCA through the Compassionate Access Program) may be supplied by companies outside of Canada.
- NOTE: Inclusion of an indication in this section does not imply that it is a BCCA approved indication.

### SPECIAL PRECAUTIONS:

- Includes special considerations for identifying patients who should NOT receive a drug or should receive it with cautions or dose adjustment.
- This section is abbreviated compared to the full CDM monograph and does not contain information about carcinogenicity, pregnancy, fertility, etc.

### SIDE EFFECTS:

- Includes adverse events that may present during drug treatment but do not necessarily have a causal relationship with the drug, as well as adverse reactions that are suspected to be related to the drug.<sup>1,2</sup>
- Includes primarily acute reactions
- Side effects are presented in table format; selected side effects may be described in greater detail in paragraphs after the table.
- Side effects are categorized according to the US National Cancer Institute *Common Terminology Criteria for Adverse Events (CTCAE)* and *Common Toxicity Criteria (CTC)*<sup>1</sup>, with the exception of febrile neutropenia which is included in the *blood/bone marrow* category for ease of cross-reference between course of neutropenia and infection.
- Other features of the table include:
  - *Extravasation hazard* is classified as vesicant, irritant, or none. See Extravasation Policy for definitions.
  - *Emetogenic potential* is classified according to the percentage of patients who will vomit without antiemetics: high (> 90%); high moderate (60-90%); low moderate (10-60%); non-emetogenic (< 10%). See SCNausea protocol.
  - Frequency for overall (all grades) and severe (grade 3 or 4) side effects are reported when known.
  - Clinically significant or dose limiting side effects are in ***bold and italics***.

### INTERACTIONS:

- Evidence-based drug-drug, drug-herb, and drug-food interactions are listed in the interaction table, including details regarding the outcome of the interaction, mechanism, and management strategy.
- Interactions due to obvious, simple additive or antagonistic effects based on known pharmacologic activity of the interacting agents are not included.<sup>4</sup>
- Theoretical interactions may be included below the interaction table if considered potentially clinically significant.
- Grapefruit interactions are included; however, interactions with other foods susceptible to interaction (i.e., pomelo, lime, bitter orange, etc.) are not routinely included as this information is not readily available in standard references and the clinical significance is unknown.

### **SUPPLY AND STORAGE:**

- Identifies available pharmaceutical products and storage; includes inactive ingredients of potential clinical significance.<sup>5-7</sup>
- For basic information on the current brand used at the BCCA, refer to Chemotherapy Preparation and Stability Chart for details.

### **SOLUTION PREPARATION AND COMPATIBILITY:**

- Identifies information pertinent to the safe preparation of the drug.
- For basic information on preparation and administration of the current brand used at the BCCA, refer to Chemotherapy Preparation and Stability Chart for details.
- For details relating to physicochemical compatibility details, readers should consult current specialty references dealing specifically with injectable drugs.

### **PARENTERAL ADMINISTRATION:**

- Includes commonly used routes and rates of administration, as well as routes that are relatively or absolutely contraindicated.
- Routes and rates of administration approved for use at BCCA are in ***bold and italics***. Refer to the CAP approval by which a patient is being treated.

### **DOSAGE GUIDELINES:**

- Inclusion of a dosing regimen in this section does not imply efficacy or safety for a particular indication.
- Includes the most common average dosage range for parenteral routes of administration in adults. Refer to the CAP approval by which a patient is being treated.
- Dosing regimen information is generally based on the recommendations of the US National Institutes of Health and National Cancer Institute<sup>8</sup>:
  - cycle length,
  - dosage (usually expressed per body surface area or weight),
  - amount of drug per dose and range,
  - frequency of administration and/or days on which the drug is given, and
  - total dose per cycle and range.

### **REFERENCES:**

- Identifies cited references used in the writing of the interim monograph.

### **APPENDICES to the BCCA CANCER DRUG MANUAL:**

- Includes ancillary information on selective support medications, antiemetic drugs, administration guidelines, safe handling of cytotoxics and wastes, extravasation, hypersensitivity reactions, etc.

#### ***Chemotherapy Preparation and Stability Chart:***

- Provides basic information for the preparation and stability of parenteral drugs prepared and administered at BCCA. See User's Guide to the BC Cancer Agency Chemotherapy Preparation and Stability Chart for details.

#### ***Hazardous Drug List:***

- Identifies drugs which are considered hazardous at the BCCA; including drugs on the current published NIOSH HD list, as well as drugs not otherwise evaluated by NIOSH but which have been evaluated as hazardous by BCCA using the NIOSH criteria. See BCCA Provincial Pharmacy Directive VI-80: Hazardous Drug List.

- Includes only those drugs approved for use at BCCA regional centres as per the BCCA Benefit Drug List or via the BCCA Compassionate Access Program (CAP). For non-oncology drugs, refer to the current published NIOSH List.

***Extravasation Hazard Table:***

- Identifies the extravasation hazard (described as vesicant, irritant, and none) for oncology drugs available at the BCCA. See BCCA Policy III-20 Prevention and Management of Extravasation of Chemotherapy.

**REFERENCES:**

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5. CYP3A. In: Levy RH, Thummel KE, Trager WF, Hansten PD, Eichelbaum M, editors. Metabolic drug interactions. Philadelphia, PA: Lippincott Williams and Wilkins; 2000. p. 115-34.
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8. Anonymous. "Inactive" ingredients in pharmaceutical products: update. Pediatrics 1997;99(2):268-78.
9. Napke E. Excipients, adverse drug reactions and patients' rights. Can Med Assoc J 1994;151(5):529-33.
10. Kohler D, Montello M, Green L, et al. Standardizing the expression and nomenclature of cancer treatment regimens. American Society of Health-System Pharmacist (ASHP), American Medical Association (AMA), American Nurses Association (ANA). Am J Health Syst Pharm 1998;55(2):137-44.